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Effect of blood perfusion on diffusive transport in peritoneal dialysis

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Background. Diffusive transport between blood and dialysate during peritoneal dialysis is evaluated in clinical and experimental studies by the diffusive mass transport coefficient, K_{BD}. This global parameter depends on the local diffusive characteristics of the blood capillary wall (permeability) and the tissue, as well as on the density and distribution of capillaries within the tissue. It also depends on the rate of delivery (or washout) of solutes from the tissue with blood flow, that is, on the rate of tissue perfusion. However, the role of blood perfusion in peritoneal transport has not been theoretically evaluated.

Methods. The relationship between the local characteristics of the peritoneal tissue and the global diffusive mass transport coefficient was studied using a new extended version of the distributed model for peritoneal transport, which included the effect of tissue perfusion and capillary surface area on the blood–tissue transport.

Results. The solute concentration profiles within the tissue were found to depend on the solute penetration depth, which is equal to the square root of the ratio of the solute diffusivity in tissue to the solute clearance from the capillary bed to tissue. It was shown that K_{BD} might be interpreted as the dialysance of a capillary bed of a characteristic size that would be immersed directly in dialysate. A definition of the effective peritoneal blood flow (EPBF; the blood flow within the tissue layer) was formulated, and it was shown that EPBF depends on the local transport characteristics for the solute. Assuming typical values of the model parameters (known from physiological studies), the values of K_{BD} and EPBF for urea, creatinine, glucose, and CO_2 were calculated and compared with the measured values with good qualitative agreement. The transient initial increase of K_{BD} values observed at the beginning of the peritoneal dialysis dwell was interpreted as a transient sixfold increase in tissue perfusion and a twofold increase in the capillary surface area.

Conclusion. The distributed model can be useful as a theoretical tool for detailed physiological interpretations of changes in peritoneal transport associated with changes in peritoneal microcirculation and structure of the interstitium.

Key words: mathematical model, small solutes, peritoneal membrane, transport, blood flow, dialysate.

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The role of blood flow in transport of solutes and water between blood in the capillary blood vessels and dialysate during peritoneal dialysis has been discussed since the onset of this therapy [1]. In general, the transport rates for small solutes and water from blood to dialysate depend on the rate of their supply to peritoneal tissue with blood flow or, in the case of transport from the dialysate to blood, on the rate of their removal with blood flow from peritoneal tissue. However, the quantitative importance of blood flow has not yet been established.

Based on the estimation of the effective blood flow rate with clearance of a quickly diffusive gas, some investigators have suggested that blood flow is fast enough not to limit the peritoneal transport of small solutes [1–3]. This assumption made it possible to consider blood as a well-mixed compartment in modeling of peritoneal transport. On the other hand, other arguments have also been formulated suggesting that the effective blood flow rate may be small enough to limit the transport of small solutes [1, 4].

The objective of this study was to clarify the problem of the effect of blood flow on peritoneal transport using mathematical models of solute transport through permselective membranes. The modeling includes the description of the transport between capillary blood and interstitial fluid, as well as the spatial distribution of capillaries inside the submesothelial tissue. The proposed approach is based on two methods developed in physiology: (*a*) the indicator dilution method for the investigation of the transport of solutes through the capillary wall [5–7], and (*b*) the distributed model of the solute transport between blood passing through an organ and external (to the organ) medium (such as the peritoneal dialysate) [8, 9]. The results are interpreted in the terms of a widely used phenomenological approach that is based on the assumption of well-mixed blood and dialysate compartments and a single layer of permselective membrane between these compartments [10, 11].

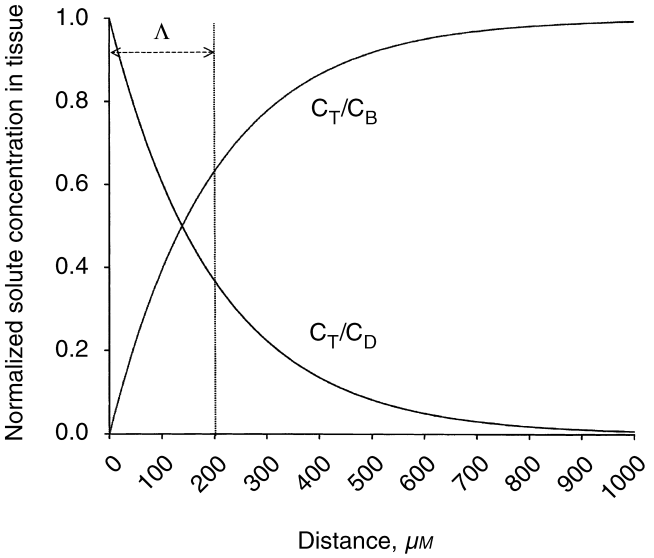

Fig. 1. Normalized solute concentration profiles within tissue, C_T/C_D for the transport from dialysate to blood with blood concentration equal to zero, and C_T/C_B for the transport from blood to dialysate with dialysate concentration equal to zero, calculated using equation 2 for the penetration depth Λ = 200 μm. Distance zero means the surface of the tissue.

METHODS AND RESULTS

Characteristics of diffusive peritoneal transport according to the distributed model

Blood capillaries are located within the submesothelial tissue at various distances from the peritoneal surface. The difference in solute concentration between blood and dialysate induces a continuous concentration profile within the tissue that changes from a value of the solute concentration C_T equal to the dialysate concentration at the mesothelial cell layer (C_D) to a value approaching the concentration of the solute (C_B) in blood that enters the tissue capillaries (Fig. 1). Therefore, the concentration of the solute outside of a capillary depends on the distance of this capillary from the peritoneal surface. This fact has been taken into account in the so-called distributed model of peritoneal transport [8], but is neglected in other mathematical models, such as the membrane model [11] or the three-pore model [10]. Later in this article we discuss a new version of the distributed model, which takes into account the blood flow within the capillaries in peritoneal tissue.

Diffusion (*a*) between blood and interstitial fluid, (*b*) through interstitial fluid and, possibly, through the tissue cells, and (*c*) between the tissue and dialysate is the main transport component for most low and medium molecular weight solutes. In contrast, convective transport plays a more important role for macromolecules, and therefore, the description of macromolecular transport is out of the scope of this study [10].

Diffusive transport through the capillary wall. The diffusive mass transport coefficient, K_{BT}, between blood and surrounding tissue is usually expressed per unit volume (or equivalently, per unit weight) of the tissue; such normalized parameter is denoted by k_{BT}. In the same way, the capillary surface area, A_c, and the rate of blood flow, Q_B, normalized to the unit volume/weight of the tissue is denoted a_c and q_B, respectively. According to a standard model applied in the studies of solute transport between blood and tissue, the diffusive mass transport coefficient depends on capillary wall diffusive permeability, P_c, capillary surface area, a_c, and perfusion rate, q_B, in the following manner [5–7, 12–18]:

$$k_{BT} = q_B[1 - \exp(-P_c a_c/q_B)] \qquad \text{(Eq. 1)}$$

If $P_c a_c \gg q_B$ (blood flow-limited transport), then k_{BT} is proportional to q_B, whereas for solutes with $P_c a_c \ll q_B$ (permeability-limited transport), k_{BT} is proportional to $P_c a_c$.

Diffusive transport through the tissue. The rate of diffusive transport through the tissue is described as the diffusivity, D_T.

Diffusive transport in peritoneal dialysis. The transport through the capillary wall and tissue depends on two parameters, k_{BT} and D_T. Considering the transport from dialysate to blood, the solute enters the tissue and diffuses from the surface to deeper layers of the tissue. However, it may also enter blood capillaries and be washed out from the tissue. In the steady state, a characteristic concentration profile arises, as the concentration of the solute decreases with the distance from the surface as a result of the washout. If it were not for this washout, the solute would saturate the tissue at the level of equilibrium with the dialysate. In the case of marked washout, the solute may not even be able to penetrate deep to the tissue. The penetration depth is characterized by the parameter Λ, which, according to the distributed model, may be calculated from this equation: $\Lambda = \sqrt{D_T/k_{BT}}$ [8].

In most cases of interest in peritoneal dialysis, the concentration profile within the tissue is exponential [8]:

$$C_T = C_B + (C_D - C_B)\exp(-z/\Lambda) \qquad \text{(Eq. 2)}$$

where z denotes the distance from the surface of the tissue (that is, the mesothelium–dialysate border). The penetration depth, Λ, for the transport from dialysate to blood denotes the distance from the tissue surface at which the concentration decreases to 37% [note that $\exp(-z/\Lambda) = 0.37$ for $z = \Lambda$] of the dialysate concentration (assuming that the solute concentration in systemic blood is close to zero; Fig. 1). In the same way, if the solute diffuses from blood to dialysate, its concentration in deep tissue layer is, in the steady state, in equilibrium with its concentration in blood, but close to the surface, it decreases to reach the equilibrium value with the con-

centration in dialysate. The mathematical description of the concentration profile is also given by equation 2. The penetration depth Λ now denotes the distance from the tissue surface at which the concentration is equal to 63% [note that $1 - \exp(-z/\Lambda) = 0.63$ for $z = \Lambda$] of blood concentration, C_B, assuming that the solute concentration in dialysate is close to zero (Fig. 1).

Transport parameters

Analysis of available data about tissue diffusivity and permeability of the capillary wall for small hydrophilic solutes provides insight into the possible range of the transport parameters for the distributed model. Furthermore, the transport of lipophilic gases, as CO_2, which play an important role in the assessment of the effective blood flow in peritoneal dialysis, is also evaluated.

Blood–tissue exchange of solutes. Diffusive permeability through the capillary wall, P_c, for the mammalian muscle may be described as a function of the molecular weight (MW): $P_c = 296 \times MW^{-0.63} \times 10^{-6}$ cm/second for hydrophilic solutes of the size ranging from MW = 60 (urea) to 5000 (inulin) [8].

The lowest possible perfusion rate (q_B) in the resting muscle was reported to be approximately 0.01 to 0.03 ml/min per 1 g of the tissue, but the typical value is often assumed to be 0.06 ml/min/g or higher [9, 19, 20]. For example, feline splanchnic perfusion rates measured with Tyrode's solution in the peritoneal cavity were 0.062 for parietal wall, 0.063 for omentum, 0.054 for mesentery, and 0.097 ml/min/g for intestinal serosa [20]. In the hard-working muscle, perfusion may increase up to 1 ml/min/g [21]. Blood perfusion for the liver was estimated as 0.83 ml/min/g and for the other viscera as 0.65 ml/min/g [9].

The density of the capillary surface area (a_c) was assumed to be equal to 70 cm^2 per 1 g of the tissue, as measured for the resting muscle [9]. However, the number of open capillaries and, therefore, their total surface density may change because of physiological or pharmacological factors [1]. In particular, a_c may increase twofold to threefold above the typical value if perfusion increases to its highest rate [21]. On the other hand, for low blood flow, the heterogeneity of the vascular bed (that is, the variability of the capillary length) may result in an approximately twofold decrease in the permeability–surface area product [17, 18]. Therefore, we use the reference value $a_{c0} = 70$ cm^2/g of the tissue for $q_B = 0.15$ ml/min/g, and $a_c = 0.5\ a_{c0}$ for $q_B = 0.01$, $a_c = 0.75\ a_{c0}$ for $q_B = 0.06$, $a_c = 1.5\ a_{c0}$ for $q_B = 0.30$, and $a_c = 2\ a_{c0}$ for $q_B = 0.60$ ml/min/g. The coefficients in these relationships of a_c to a_{c0} were selected to adjust the values of a_c to the measured values of $P_c a_c$ as a function of q_B [18].

The diffusive permeability of the capillary wall for the lipophilic gases is so high (for example, $P_c = 3$ cm/second for O_2) that their k_{BT} values are practically equal to q_B (compare with equation 1) [22, 23]. Thus, the transcapillary transport of lipophilic gases may be considered as flow limited.

Tissue transport. Tissue diffusivity, D_T, may be described as the function of MW: $D_T = 0.036 \times D_W$, where $D_W = 10.18 \times MW^{-0.45} \times 10^{-5}$ cm^2/second is the solute diffusivity in water for small hydrophilic solutes [8]. For lipophilic solutes, the tissue diffusivity (D_T) was found to be between one third and two thirds of the respective diffusivities in water [22]. The diffusion coefficient D_W for CO_2 in water is equal to 1.77×10^{-5} cm^2/second [22], and D_T may be approximately described as $D_T = 0.5 \times D_W$.

Diffusive mass transport coefficient in peritoneal dialysis

The diffusive mass transport coefficient (K_{BD}) for peritoneal dialysis is described according to the distributed model, as follows [8]:

$$K_{BD} = A_M\sqrt{D_T k_{BT}} \qquad \text{(Eq. 3)}$$

where A_M is the surface area of the contact with dialysate. Using the description of Λ as $\Lambda = \sqrt{D_T/k_{BT}}$ (discussed earlier in this article), one may express equation 3 in two other (but equivalent) ways:

First, K_{BD} is equal to the diffusive mass transport coefficient for the exchange between blood and tissue, $K_{BT,\Lambda}$, within the layer of the width Λ, that is, to k_{BT} multiplied by the volume of the layer $V_\Lambda = \Lambda A_M$:

$$K_{BD} = k_{BT}\Lambda A_M \qquad \text{(Eq. 4)}$$

This formula for K_{BD} means that peritoneal dialysis (restricted to pure diffusive transport) may be considered as the direct diffusive exchange of the solute between dialysate and blood microcirculation in an apparent tissue layer of width Λ.

Second, K_{BD} is equal also to the diffusive permeability, $K_{T,\Lambda} = P_{T,\Lambda}A_M$, where $P_{T,\Lambda} = D_T/\Lambda$, for diffusion of the solute through a tissue layer of the width Λ, as there would be no capillaries with blood flow within it, that is:

$$K_{BD} = (D_T/\Lambda)A_M \qquad \text{(Eq. 5)}$$

Note, however, that Λ, which appears in equations 4 and 5, depends on D_T and k_{BT} and is different for different solutes.

Effective peritoneal blood flow

In the context of peritoneal dialysis, it is usually assumed that only a relatively thin layer of the tissue that is adjacent to the peritoneal surface participates effectively in the exchange of solutes between dialysate and blood [1]. The rate of blood flow in this layer is called the effective peritoneal blood flow (EPBF). Some investigators attempted to evaluate EPBF using quickly diffusing gases; others considered the gas clearances as an overes-

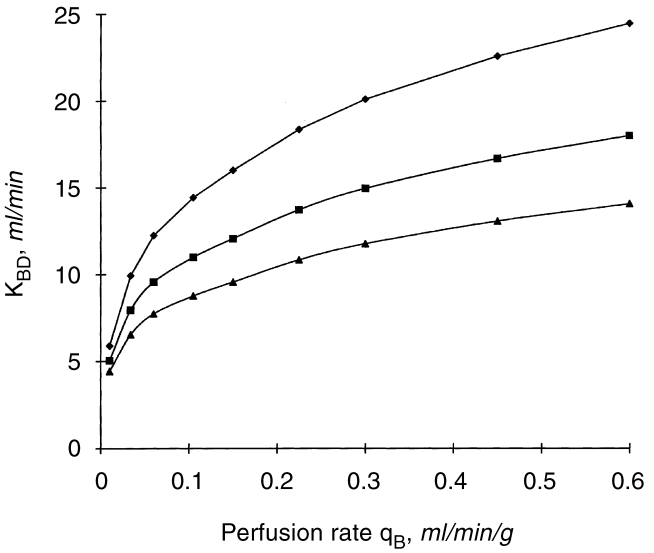

Fig. 2. Diffusive mass transport coefficient for peritoneal dialysis (K_{BD}) for small hydrophilic solutes as a function blood perfusion rate, q_B, for the total peritoneal surface area A_M = 1.0 m². Symbols are: (◆) urea; (■) creatinine; (▲) glucose.

timation of EPBF and pointed out the possibility of much lower values for EPBF as well as different EPBF values for solutes of different transport characteristics [1, 4, 24].

The distributed model provides a precise measure of the tissue layer involved effectively in peritoneal dialysis. Because the diffusive transport in peritoneal dialysis may be considered as a direct exchange of a solute between dialysate and blood in the tissue layer of the penetration depth, Λ, we can define the EPBF for the solute as the blood flow rate within this tissue layer of the volume $V_\Lambda = A_M\Lambda$, that is:

$$Q_{BEF} = q_B\Lambda A_M \qquad \text{(Eq. 6)}$$

The so-defined EPBF is different for different solutes.

Effect of perfusion on peritoneal transport

The diffusive mass transport coefficients, K_{BD}, and the EPBFs, Q_{BEF}, for various solutes may be calculated using the distributed model and compared with their values measured in the peritoneal dwell studies. However, peritoneal dialysate is in contact with many different organs, each characterized by its own transport and geometric parameters, and the value of K_{BD} should be estimated as the sum of the diffusive mass transport coefficients for each of these organs. Such an approach, although possible [25], is burdened with the uncertainty of the values of the organ-specific parameters [26]. Therefore, one can attempt to assume the transport and geometric parameters for the "average" peritoneal tissue, calculate K_{BD} values, and compare them with K_{BD} values measured in clinical dwell studies. However, the knowledge of many important parameters is far from being unequivocal. The total peritoneal surface area is believed to be equal to the total body surface, that is, to 1.75 m² in average. However, direct measurements yielded lower values: 1.04 [27], 0.78 (without the mesentery) [28], and 1.3 m² [29]. We chose rather arbitrarily 1.0 m² as the reference value for the total peritoneal surface area. The theoretical description of diffusive mass transport coefficients, K_{BD}, as the function of perfusion rate, q_B, for urea, creatinine, and glucose is shown in Figure 2. Fitting the values of the diffusive mass transport coefficient, K_{BD}, calculated using equation 3, to the values measured during peritoneal dialysis in continuous ambulatory peritoneal dialysis (CAPD) patients, one can do the evaluation of the tissue perfusion.

Table 1. Theoretical values of the diffusive mass transport coefficient (K_{BD}) calculated from the distributed model and values of K_{BD} measured in clinical studies

	K_{BD} ml/min				
	Theoretical[a]		Clinical		
	q_B = 0.30	q_B = 0.05		Time dependent[b]	
	Initial	Final	Time averaged	Initial	Final
CO_2	136.1	55.6	75[c]–159[d]		
Urea	19.8	11.3	21[e]	30.9	18.9
Creatinine	14.7	8.8	10[e]	14.8	8.8
Glucose	11.6	7.2	10[e]	13.5	8.0

[a] q_B, blood flow per unit of tissue volume (ml/min/g)
[b] From [31]
[c] Measured for 6-hour exchange, from [32]
[d] Measured at the beginning of the exchange, from [33]
[e] Mean values from eight different studies summarized in [11]

Diffusive mass transport coefficients, K_{BD}, are not constant during a single CAPD exchange with standard glucose-based solutions, but they are higher at the beginning than at the end of the exchange [30, 31]. Evaluation of these "time-dependent K_{BD} values" showed that for small solutes (as urea, creatinine, and glucose), the values of K_{BD} decreased exponentially during the CAPD exchange and reached the final steady-state value after approximately three hours [30, 31]. The initial K_{BD} values were higher by approximately 60% than the final ones. This phenomenon was observed for CAPD exchanges with the standard glucose-based dialysis fluid, but not for exchanges with other experimental dialysis fluid of different composition, and was attributed to a (hypothetical) change of tissue perfusion during the course of the peritoneal exchange due to vasodilatory factors in dialysis fluid [31].

In Table 1, mean values of K_{BD}, as summarized by Lysaght and Farrell [11], are shown, as well as the initial and the final K_{BD} values during CAPD exchanges with the standard dialysis fluid. The values of K_{BD}, which were matched using the distributed model to the measured values, are also shown in Table 1. The selection of the two perfusion rates was done to get an acceptable agreement

Table 2. Theoretically estimated transport characteristics for a peritoneal tissue of 1.0 m^2 surface

	q_B = 0.30 ml/min/g			q_B = 0.05 ml/min/g		
	Λ *mm*	K_{BD} *ml/min*	Q_{BEF} *ml/min*	Λ *mm*	K_{BD} *ml/min*	Q_{BEF} *ml/min*
CO_2	0.39	136.1	136.1	0.95	55.6	55.6
Urea	0.18	19.8	52.7	0.31	11.3	15.4
Creatinine	0.18	14.7	53.8	0.30	8.8	14.9
Glucose	0.19	11.6	55.1	0.30	7.2	14.8

Abbreviations are: qB, blood flow per unit of tissue volume; Λ, penetration depth; K_{BD}, diffusive mass transport coefficient; Q_{BEF}, effective peritoneal blood flow.

between theoretical and time-dependent K_{BD} values for creatinine, which seems to well represent small lipid insoluble solutes. In that way, one may state that the perfusion in the "equivalent" layer of the peritoneal tissue was 0.30 ml/min/g at the beginning of the exchange and decreased to 0.05 ml/min/g at the end of the six-hour exchange. This steady-state value of perfusion is very close to the value 0.06 ml/min usually assumed for the resting muscle [26], but the initial value is six times higher and characteristic for the diaphragm [26]. The penetration depth and EPBF for the discussed solutes and the selected perfusion rates are shown in Table 2.

As shown in Table 1, there was a good agreement between theoretical and clinical values of K_{BD} for creatinine (MW = 111). For other solutes, there were some discrepancies as discussed later here.

CO_2 (molecular weight = 44). The values of diffusive mass transport coefficients, K_{BD}, for quickly diffusing, lipid-soluble gases are considered to be a measure of EPBF [1]. In clinical studies, the transport of CO_2 only was evaluated [24, 32]. Nolph et al found a very fast increase of CO_2 concentration in dialysate using commercial dialysis fluid during CAPD exchanges and interpreted this phenomenon as local generation of CO_2 caused by low pH of the fluid [32]; local CO_2 generation was also found in experimental peritoneal dwell studies in rats [3]. Therefore, pH-neutralized dialysis solution was applied, and K_{BD} values for CO_2 during a six-hour exchange were found to be between 68 and 82 ml/min (mean value of 75 ml/min is shown in Table 1). Recently, K_{BD} values for CO_2 within the range 20 to 137 ml/min (median 60 ml/min) if measured with the standard (but pH neutral) glucose-based dialysis fluid, but significantly higher if measured with amino acid-based dialysis fluid (within the range 57 to 187 ml/min, median 93 ml/min) were reported by Douma et al [33]. The increased diffusive transport of CO_2 and other small solutes with amino acid-based fluid was attributed to a vasodilatory effect of this fluid [15]. In contrast, the evaluation of CO_2 transport during repeated short exchanges with intermittent peritoneal dialysis treatment did not show any significant differences between acidic and neutralized dialysis fluids [24]. Furthermore, the measured K_{BD} values were much higher (approximately 159 ml/min; Table 1; or even higher in later studies, 223 ml/min [34]) than those reported by Nolph et al [32] and Douma et al [33]. However, these high K_{BD} values were measured during a short (2.5 to 3 min) period immediately after the infusion of dialysis fluid, which may involve some system-related errors, as nonsteady state of transport, imperfect mixing of the infused and residual fluid, etc. The difference between K_{BD} values for CO_2 found in CAPD [32] and in intermittent peritoneal dialysis [24] might also be caused by different treatment regimes and therefore different response of the peritoneal tissue to stimulae from dialysis fluid.

Urea (molecular weight = 60). The ratio of the measured K_{BD} values between urea and creatinine is higher than 2.0, whereas the ratio of theoretical values for these two solutes is approximately 1.3. In our calculations, we assumed the capillary permeability and tissue diffusivity for urea according to the formula established for solutes of MW from the size of urea to the size of inulin (discussed earlier in this article). However, water diffusivity for urea is higher by approximately 20% than predicted by the formula used in this study (Fig. 2 in [8]). Furthermore, urea is known to diffuse rapidly through lipid membranes, in contrast to creatinine and bigger lipid-insoluble solutes [35]. Therefore, we may expect that tissue diffusivity and capillary permeability for urea may be much higher than predicted here. In fact, a twofold increase of D and P_c for urea yields K_{BD} values equal to 18.0 and 35.7 ml/min for q_B = 0.05 and 0.30 ml/min, respectively, in agreement with the measured time-dependent values (Table 1).

Glucose (molecular weight = 180). The K_{BD} values reported for glucose were usually close to those for creatinine (time average values; Table 1), in spite of higher molecular mass for glucose than for creatinine. The time-dependent K_{BD} values were approximately 10% higher for creatinine than for glucose (time-dependent values; Table 1). However, theoretical predictions yield K_{BD} for creatinine approximately 22 to 26% higher than for glucose (theoretical values; Table 1). This suggests that glucose-diffusive transport is higher than expected, perhaps because of (some small component of) active transport across (and/or into) cells. It is worth noting that glucose transport was evaluated in the cited studies for dialysate containing unphysiologically high glucose concentrations.

DISCUSSION

The changes over time in the values of K_{BD} throughout the single CAPD exchange of standard glucose-based dialysis fluid may be explained by the changes in blood perfusion of the abdominal organs [31]. This hypothesis

was investigated in this study, and the predicted increase in blood perfusion required to explain the observed change in K_{BD} values was sixfold: from 0.05 to 0.30 ml/min/g (discussed earlier in this article). According to the model, this was accompanied by a twofold increase in the capillary surface area.

The impact of dialysis solution on the blood flow in the abdominal organs was studied in the cat using the microsphere technique as well as by electromagnetic flowmetry [20]. No significant change in blood flow through the celiac and superior mesenteric arteries was observed. Furthermore, no change in the blood perfusion of the major abdominal organs (liver, stomach, intestine, pancreas, and spleen) was found either. However, a considerable increase of blood flow to the "thin" organs has been reported [20]—for example, the mesentery (125 and 240% with Dianeal 1.36 and 3.86%, respectively, compared with the blood flow with Tyrode's solution infused to the peritoneal cavity), omentum (75 and 150%), intestinal serosa (260 and 1000%), and parietal peritoneum (75 and 150%). These experimental data suggest that substantial changes in the local peritoneal blood flow may indeed occur during peritoneal dialysis. They may be explained by the vasodilatory effect of the dialysis fluids on a rather thin tissue layer, which is in contact with dialysis fluid, in agreement with a low penetration depth of vasoactive factors in dialysis fluid, such as glucose, lactate, etc. [20]. This effect may induce a redistribution of blood flow to this thin layer rather than an increase of blood flow in the abdominal area. However, the vasodilated layer constitutes a large part of "thin" organs, and the total blood flow to such an organ therefore increases. In contrast, in "thick" organs, this layer forms a small part of the organs; the redistribution of blood flow may occur without any considerable increase in the total blood flow to the organ, and vice versa, the changes in the total blood flow to an organ do not necessarily need to induce considerable changes in the perfusion of the tissue layer that participates in the exchange of solute with dialysate in the peritoneal cavity. In conclusion, one may expect a severalfold increase of blood flow within a thin tissue layer in contact with dialysate, and perhaps a "distributed profile of blood perfusion" within this layer with perfusion rate decreasing with the distance from the organ surface in agreement with the concentration profile of the vasodilatory agent(s). The assumption of uniform blood perfusion used in our modeling may therefore need a modification if a more precise theoretical description of the peritoneal transport is to be provided.

The impact of vasoactive substances on the peritoneal transport was addressed in numerous studies [26, 36]. It is not possible here to discuss all issues related to the topic. Nevertheless, it is worth noting that many vasoactive solutes increase the peritoneal transport only if they are applied *in situ*, that is, added to dialysis fluid, but not if they are infused into the systemic circulation [26, 36]. This observation confirms indirectly that the peritoneal transport depends on perfusion of a thin tissue layer in contact with the peritoneal dialysate.

Our approach uses the theoretical concept of the apparent "average" peritoneal tissue layer with homogeneous transport characteristics and attempts to quantitate some parameters that are often applied for the presentation and discussion of the peritoneal transport and peritoneal dialysis. This concept may provide some insight into the typical behavior of the tissue, which participates in the solute exchange during peritoneal dialysis. In fact, most of the theoretical work on the peritoneal transport, including the membrane model, the three-pore model and some of the previous applications of the distributed model, deal with such an "average" peritoneal tissue.

The distributed model provides physiological interpretations for the diffusive mass transfer coefficient, K_{BD}, and for the EPBF in the terms of the tissue perfusion and the local transport parameters for the tissue and for the blood capillary wall. The model yields reasonably good agreement between the calculated and the measured values of K_{BD}, in spite of many simplifications included into the distributed modeling and into the idea of the apparent layer of the peritoneal tissue. We may expect that further applications of the model for analyses of clinical and experimental studies on the peritoneal diffusive transport will contribute to a better understanding of the peritoneal transport physiology.

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APPENDIX

Abbreviations are: A_c, total capillary surface area, cm^2; A_M, total peritoneal surface area, m^2; a_c, density of total capillary surface area, cm^2/g; C_B, solute concentration in blood, mmol/ml; C_D, solute concentration in dialysate, mmol/ml; C_T, solute concentration in tissue, mmol/ml; D_T, solute diffusivity in tissue, cm^2/second; D_W, solute diffusivity in water, cm^2/second; K_{BD}, net diffusive mass transport coefficient in peritoneal dialysis, ml/min; K_{BT}, diffusive mass transport coefficient for blood–tissue solute exchange, ml/min; $K_{BT,\Lambda}$, K_{BT} for a tissue layer of the width Λ, ml/min; $K_{T,\Lambda}$, diffusive mass transport coefficient for solute transport through a tissue layer of width Λ, ml/min; k_{BT}, K_{BT} expressed per unit tissue volume/weight, ml/(g · min); MW, molecular weight; P_c, diffusive permeability for capillary wall, cm/second; $P_{T,\Lambda}$, diffusive permeability through the tissue layer of width Λ; Q_B, blood flow, ml/min; Q_{BEF}, effective blood flow, ml/min; q_B, density of blood flow (perfusion rate), ml/(g · min); V_Λ, volume of the tissue layer of

width Λ, ml; z, distance in the tissue from the peritoneal surface, cm; and Λ, penetration depth, cm.

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